THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Appellants:	Troup, et al.
Appl. No.:	10/662,678
Conf. No.:	1877
Filed:	September 15, 2003
Title:	NUTRITIONAL COMPOSITIONS
Art Unit:	1654
Examiner:	Julie Ha
Docket No.:	3712036-01326

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

APPELLANTS' REPLY BRIEF

Sir:

I. INTRODUCTION

Appellants submit Appellants' Reply Brief in response to the Examiner's Answer dated July 11, 2011 pursuant to 37 C.F.R. § 41.41(a). Appellants respectfully submit that the Examiner's Answer has failed to remedy the deficiencies with respect to the final Office Action dated November 24, 2010, as noted in Appellants' Appeal Brief filed on April 21, 2011, for at least the reasons set forth below. Accordingly, Appellants respectfully request that the rejection of pending Claims 1-4, 7-11, 13-14, 16-17, and 23-28 be reversed.

II. THE REJECTION OF CLAIMS 1-4, 7-11, 13-14, 16-17, AND 23-28 UNDER 35 U.S.C. §103(a) SHOULD BE REVERSED BECAUSE THE EXAMINER HAS FAILED TO ESTABLISH A PRIMA FACIE CASE OF OBVIOUSNESS

Appellants respectfully request that the Board reverse the rejection of Claims 1-4, 7-11, 13-14, 16-17, and 23-28 under 35 U.S.C. §103(a) because the Examiner has still failed to establish a *prima facie* case of obviousness with respect to the cited references.

In the Examiner's Answer, the Examiner argues that "the primary reference [*Abbruzzese*] teaches all of the active components of the present claims." Examiner's Answer, page 26. Yet, what the primary reference fails to teach is the amounts of these active components which are recited in the present claims. Specifically, *Abbruzzese*, as well as the cited secondary references *Roberts*, *Hageman*, *Salvati*, and *Vickery*, all fail to disclose, at least, compositions having leucine, valine in an amount of about 8% to about 10% by weight based on the weight of total amino acids, and at least one essential amino acid selected from the group consisting of isoleucine, lysine, methionine, phenylalanine, threonine, tryptophan, histidine, and combinations thereof in free and/or salt form, wherein said leucine is in free and/or salt form as required, in part, by independent Claims 1-3, 17, 23-25 and 28.

It is undisputed that *Abbruzzese* does not disclose or suggest compositions containing about 8% to about 10% of valine as required, in part, by the present claims. Indeed, at best, *Abbruzzese* discloses only 5.9% valine. See, *Abbruzzese*, Table 4. It is similarly undisputed that *Roberts*, *Hageman*, and *Salvati* also do not disclose or suggest compositions containing about 8% to about 10% of valine as required, in part, by the present claims. Indeed, at best, *Hageman* discloses only 3.5% valine. See, *Hageman*, Example 2. The Examiner also does not argue that these references teach the required amount of valine.

Instead, the Examiner points to *Vickery* for disclosure of valine in the claimed amount. As previously noted, *Vickery* does disclose valine in an amount of 7% to 10% of the weight of the total active ingredients in the composition. See, *Vickery*, column 4, lines 49-53. This is in contrast to the current claims, which require 8% to 10% valine by weight of the total amino acids in the composition.

Specifically, the Examiner looks to column 2, lines 8-30 in *Vickery* for a list of components in a preferred embodiment. From this list, using the minimum percentage of all the components given, the Examiner calculates that there would be "about 7.8% (about 8%) L-valine

based on the weight of total amino acids." See, Examiner's Answer, page 29. From this the Examiner concludes that "*Vickery* teaches the instant L-valine amount recited in the instant claims." See, Examiner's Answer, page 29.

Yet, what the Examiner has still failed to consider is that *Vickery*'s actual list of what may be considered an active ingredient is not in column 2, lines 8-30, but is instead found at column 5, lines 58-67. In this paragraph, *Vickery* further defines the "active ingredients" as including various amino acids, molybdenum, creatine, creatine monohydrate, sulfur, methylsulfonylmethane, powdered egg white or powdered milk, and powdered enzymes. See, *Vickery*, column 5, lines 58-67. As such, it is clear that the "active ingredients" of *Vickery* include at least additional creatine, sulfer, minerals, powdered dairy components and enzymes, among other ingredients. The addition of any of these components would change the overall weight of the composition from that given in column 2, lines 8-30, and change the result of the Examiner's calculation. Thus, the amounts of valine disclosed in *Vickery* are based on the "active ingredients" of the composition, and are not based on the weight of total amino acids, as is required, in part, by the present claims.

The Examiner next argues that it "would have been obvious to one of ordinary skill in the art to combine the teachings because all references teach nutritional compositions comprising differing amounts of protein and essential amino acids (such as leucine) for the same purpose (muscle enhancement)." See, Examiner's Answer, page 29. In contrast, Appellants respectfully submit that not only do the cited references fail to disclose or suggest each and every element of the present claims, they are also not obvious to combine.

Hageman, for example, does not disclose that its compound should, or even may, be used with patients suffering from anorexia or cancer cachexia. Additionally, *Hageman* is not directed towards muscle growth at all, but rather at a compound that boosts nucleotide metabolism via inclusion of both ribose and folic acid. See, *Hageman*, column 1, lines 5-10.

Further, the Federal Circuit has specifically found that references are not properly combinable or modifiable if their intended purpose is destroyed. For instance, if the proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification. *In re Gordon*, 733 F.2d 900, 221 USPQ 1125 (Fed. Cir. 1984). Since the compound in *Hageman* requires ribose and folic acid in order to boost nucleotide metabolism, the absence of ribose and

folic acid in the present claims would render the compound of *Hageman* unsatisfactory for its intended purpose, and there is no motivation to combine the teachings of *Hageman* with the other cited references in order to attempt to reach the present claims.

Regarding *Roberts* and *Salvati*, neither reference teaches that its compound should, or even may, be used with patients suffering from anorexia or cancer cachexia. Also, neither reference is directed toward muscle enhancement as the Examiner has argued.

Instead, *Salvati* generally describes fused cyclic compounds and methods of using such compounds in the treatment of nuclear hormone receptor-associated diseases such as cancer and immune disorders and pharmaceutical compositions containing such compounds. See, *Salvati*, Abstract. Appellants can find no disclosure in *Salvati* related to what the Examiner characterizes as "muscle enhancement," or to cancer cachexia. See, Examiner's Answer, page 29. This is in contrast to the present claims, which teach a compound which uses muscle protein synthesis for the control of tumor-induced weight loss, also known as cancer cachexia. See, specification, original abstract.

Additionally, *Roberts* is directed towards a balanced food composition for oral ingestion and producing low residues and diminished stoolings. See, *Roberts*, Abstract. Specifically, *Roberts* discloses a compound for use with patients experiencing an abnormal catabolic state (the body metabolizing nutrients at a rate faster than the nutrients are supplied to the body), which, when treated with natural foods, would cause residue "dumping" in the digestive tract. See, *Roberts*, column 1, lines 16-37; column 2, lines 34-55. *Roberts* teaches a compound "designed to be used as a total, nutritionally balanced single food composition . . . based on a 2,000 calorie per day intake so that patients . . . will have a nutritionally balanced diet without undue weight gain." See, *Roberts*, column 4, lines 20-28. In contrast to *Roberts*, the presently claimed compositions may be administered to:

> reduce the rate of or reverse tumor-induced weight loss, e.g. cachexia, to promote weight gain, stimulate muscle growth, enhance immune function, restore metabolic balance, support increased resistance to infection, improve tolerance to cancer therapy, enhance response to cancer therapy, reduce morbidity, improve associated symptoms that affect quality of life, such as weakness, fatigue, gastrointestinal distress, sleep/wake disturbances, pain, listlessness, shortness of breath, lethargy, depression, malaise. See, specification, page 16, lines 9-15.

Since *Roberts* expressly teaches away from one of the main objectives of the present claims, there is no motivation to combine *Roberts* with the other cited references in an attempt to teach the present claims.

In response to Appellants' argument that the claimed composition exhibited surprising results, the Examiner argues in her Answer that, in reference to Example 3, Table 4 in the original specification, there is not much difference between Leu (25%), Leu (35%), and Leu alone for protein synthesis or protein breakdown. Examiner's Answer, pages 30-31. Yet, what the Examiner has failed to recognize is that the surprising results in Example 3 are that, when leucine is present, and especially when it is 25% or 35% of an essential amino acid composition (in free and/or salt form), a stimulatory effect on net muscle synthesis is observed compared to a balanced amino acids solution containing all amino acids and a composition containing only essential amino acids. See, specification, Example 3. Specifically, the net balance for the balanced solution and the essential amino acids solution were -4.4±1.0 and -4.9±0.6, respectively. Leucine alone improved this to -2.6±0.3, but the greatest effect is observed for Leu (25%) and Leu (35%), which had a net balance of -1.2±0.2 and -1.0±0.4, respectively. See, specification, Example 3, Table 4. Appellants respectfully submit that these results do show a difference that is surprising. See, specification, page 8, lines 1-12.

For at least the above reasons, Appellants respectfully submit that *Abbruzzese*, *Roberts*, *Hageman*, *Salvati*, and *Vickery* are deficient with respect to independent Claims 1-3, 17, 23-25 and 28, and Claims 4, 7-11, 13-14, 16, and 26-27 which depend therefrom. Appellants respectfully request, therefore, that the obviousness rejections of Claims 1-4, 7-11, 13-14, 16-17, and 23-28 be reconsidered and withdrawn.

III. THE REJECTION OF CLAIMS 1-4, 7-11, 13-14, 16, AND 23-26 UNDER 35 U.S.C. §103(a) SHOULD BE REVERSED BECAUSE THE EXAMINER HAS FAILED TO ESTABLISH A PRIMA FACIE CASE OF OBVIOUSNESS

Appellants respectfully request that the Board reverse the rejection of Claims 1-4, 7-11, 13-14, 16, and 23-26 because the Examiner has still failed to establish a *prima facie* case of obviousness with respect to the cited references.

The Examiner has made the same arguments noted above in regard to the *Abbruzzese*, *Roberts*, and *Vickery* references and argued the combination of *Abbruzzese*, *Roberts*, and *Vickery* with *Allen* and *Phillips*.

Regarding the *Abbruzzese*, *Roberts*, and *Vickery* references, it is undisputed that *Abbruzzese* does not disclose or suggest compositions containing about 8% to about 10% of valine as required, in part, by the present claims. Indeed, at best, *Abbruzzese* discloses only 5.9% valine. See, *Abbruzzese*, Table 4. It is similarly undisputed that *Roberts* does not disclose or suggest compositions containing about 8% to about 10% of valine as required, in part, by the present claims. As previously noted, *Vickery* does disclose valine in an amount of 7% to 10% of the weight of the total active ingredients in the composition. See, *Vickery*, column 4, lines 49-53. But, this is in contrast to the current claims, which require 8% to 10% valine by weight of the total amino acids in the composition.

Furthermore, though the Examiner calculates that there would be "about 7.8% (about 8%) L-valine based on the weight of total amino acids," see, Examiner's Answer, page 29, the "active ingredients" of *Vickery* include at least additional creatine, sulfer, minerals, powdered dairy components and enzymes, among other ingredients. See, *Vickery*, column 5, lines 58-67. The addition of any of these components would change the overall weight of the composition from that given in column 2, lines 8-30, and change the result of the Examiner's calculation. Thus, the amounts of valine disclosed in *Vickery* are based on the "active ingredients" of the composition, and are not based on the weight of total amino acids, as is required, in part, by the present claims.

Regarding secondary references *Allen* and *Phillips*, neither reference discloses or suggests compositions containing about 8% to about 10% of valine as required, in part, by the present claims. *Allen* is entirely directed to a composition for stimulating muscle growth having an effective amount of L-arginine. See, *Allen*, Abstract. *Phillips* is cited solely for the teaching that beta-hydroxy beta-methylbutyrate (HMB) is a metabolite of leucine and may help to build muscle. See, final Office Action, page 36, lines 4-8.

Additionally, Appellants respectfully submit that not only do the cited references fail to disclose or suggest every element of the present claims, they are also not obvious to combine. *Roberts*, for example, teaches a compound "designed to be used as a total, nutritionally balanced single food composition . . . based on a 2,000 calorie per day intake so that patients . . . will have a nutritionally balanced diet without undue weight gain." See, *Roberts*, column 4, lines 20-28. In contrast to *Roberts*, the presently claimed compositions may be administered to:

> reduce the rate of or reverse tumor-induced weight loss, e.g. cachexia, to promote weight gain, stimulate muscle growth, enhance immune function, restore metabolic balance, support

> increased resistance to infection, improve tolerance to cancer therapy, enhance response to cancer therapy, reduce morbidity, improve associated symptoms that affect quality of life, such as weakness, fatigue, gastrointestinal distress, sleep/wake disturbances, pain, listlessness, shortness of breath, lethargy, depression, malaise. See, specification, page 16, lines 9-15.

Since *Roberts* expressly teaches away from one of the main objectives of the present claims, there is no motivation to combine *Roberts* with the other cited references in an attempt to reach the present claims.

The Examiner further argues that "one of ordinary skill in the art would have been motivated to optimize the concentration of different amino acids, specifically leucine, isoleucine, and valine to stimulate the muscle growth, to arrive at the optimal composition for the treatment of muscle enhancement for cancer patients." Examiner's Answer, page 36. What the Examiner fails to consider in this statement is that Appellants have surprisingly found that a formulation containing free essential amino acids as compared to a formulation containing free essential and non-essential amino acids or intact protein alone is optimal. See, specification, Examples 1-2. Appellants have also found that nutritional compositions comprising a mixture of essential amino acids in free form and/or in salt form that has particularly high amounts of leucine had a stimulatory effect on muscle protein synthesis. See, specification, Example 3.

For at least the above reasons, Appellants respectfully submit that *Abbruzzese*, *Roberts*, *Allen, Phillips* and *Vickery* are deficient with respect to independent Claims 1-3 and 23-25, and Claims 4, 7-11, 13-14, 16, and 26 which depend therefrom. Appellants respectfully request, therefore, that the obviousness rejections of Claims 1-4, 7-11, 13-14, 16, and 23-26 be reconsidered and withdrawn.

IV. THE REJECTION OF CLAIMS 1 AND 23-25 UNDER 35 U.S.C. §103(a) SHOULD BE REVERSED BECAUSE THE EXAMINER HAS FAILED TO ESTABLISH A PRIMA FACIE CASE OF OBVIOUSNESS

Appellants respectfully request that the Board reverse the rejection of Claims 1 and 23-25 because the Examiner has still failed to establish a *prima facie* case of obviousness with respect to the cited references.

The Examiner has made the same arguments noted above in regard to *Vickery*, as well as argued the combination of *Vickery* with *Heyland*. Regarding *Vickery*, the arguments discussed

above apply equally here. As previously noted, *Vickery* does disclose valine in an amount of 7% to 10% of the weight of the total active ingredients in the composition. See, *Vickery*, column 4, lines 49-53. This is in contrast to the present claims, which require 8% to 10% valine by weight of the total amino acids in the composition. Furthermore, though the Examiner calculates that there would be "about 7.8% (about 8%) L-valine based on the weight of total amino acids," see, Examiner's Answer, page 29, the "active ingredients" of *Vickery* include at least additional creatine, sulfer, minerals, powdered dairy components and enzymes, among other ingredients. See, *Vickery*, column 5, lines 58-67. The addition of any of these components would change the overall weight of the composition from that given in column 2, lines 8-30, and change the result of the Examiner's calculation. Thus, the amounts of valine disclosed in *Vickery* are based on the "active ingredients" of the composition, and are not based on the weight of total amino acids, as is required, in part, by the present claims.

The Examiner admits that *Heyland* "does not teach about 8% to about 10% valine." See, final Office Action, page 27, lines 21-22. *Heyland* discloses only essential amino acids and fails to recite any non-essential amino acids at any place in the disclosure. As such, *Heyland* also cannot disclose or suggest a ratio of total essential amino acids and, optionally, conditionally essential amino acids to total amino acids ranging from about 0.60 to about 0.90 as required, in part, by independent Claims 1 and 25.

The Examiner argues that Claims 1 and 25 do not recite any non-essential amino acids. See, Examiner's Answer, page 40. Yet, the recitation of non-essential amino acids is implicit in the ratio of essential amino acids ("EAA") to total amino acids ("TAA"). If all of the amino acids in the compound were essential, the ratio of EAA:TAA would be 1. In contrast to this, independent Claims 1 and 25 recite a ratio of EAA:TAA of 0.6 to 0.9 – notably, this ratio is less than 1. This must mean that not all of the amino acids in the compound are EAAs, and that some of the amino acids in the compound are non-essential amino acids ("NEAA"). Implicit in the claims is the recitation of the ratio of NEAA:TAA of 0.1 to 0.4. In contrast to this, *Heyland* fails to recite any non-essential amino acids at any place in the disclosure, and it cannot be considered, alone or in combination with *Vickery*, to disclose or suggest every element of the present claims.

The Examiner argues that, in reference to Example 3, Table 4 in the original specification, the results are not surprising because there is not much difference between Leu

(25%), Leu (35%), and Leu alone for protein synthesis or protein breakdown. Examiner's Answer, pages 30-31. As discussed above, what the Examiner has failed to recognize is that the surprising results in Example 3 are that, when leucine is present, and especially when it is 25% or 35% of an essential amino acid composition (in free and/or salt form), a stimulatory effect on net muscle synthesis is observed compared to a balanced amino acids solution containing all amino acids and a composition containing only essential amino acids. These results do show a difference that is surprising. See, specification, page 8, lines 1-12.

The Examiner also continues to construe "consisting essentially of" as equivalent with "comprising." See, Examiner's Answer, page 41. This is in error because, with regard to the present claims, the "consisting essentially of" language limits the composition to: containing leucine, valine and an essential amino acid (Claims 1 and 23-24), or leucine, valine, an essential amino acid and an intact protein (Claim 25), and those materials that do not materially affect the basic or novel characteristics of the claimed invention.

As noted by the Examiner, *Heyland* expressly discloses a composition having 150 g of technical leucine, 70 g of monosodium glutamate, 40 g of sodium chloride, 180 g of whey powder and 160 g of a casein hydrolysate. See, *Heyland*, column 6, lines 55-60. Appellants respectfully submit that the additional composition elements disclosed in *Heyland* materially affect the basic or novel characteristics of the claimed compositions. As such, *Heyland*, alone or in combination with *Vickery*, fails to disclose each and every element of the present claims and fails to even recognize the advantages of the presently claimed subject matter.

For at least the above reasons, Appellants respectfully submit that *Heyland* and *Vickery* are deficient with respect to independent Claims 1 and 23-25. Appellants respectfully request, therefore, that the obviousness rejections of Claims 1 and 23-25 be reconsidered and withdrawn.

In sum, not only do the cited references fail to disclose or suggest each and every element of the present claims, but the skilled artisan would have no reason to arrive at the present claims using the cited references in the absence of hindsight. Accordingly, Appellants respectfully submit that Claims 1-4, 7-11, 13-14, 16-17, and 23-28 are novel, nonobvious and distinguishable from the cited references and are in condition for allowance.

V. CONCLUSION

For the foregoing reasons, Appellants respectfully submit that the Examiner's Answer does not remedy the deficiencies noted in Appellants' Appeal Brief with respect to the non-final Office Action. Therefore, Appellants respectfully request that the Board of Appeals reverse the obviousness rejections with respect to Claims 1-4, 7-11, 13-14, 16-17, and 23-28.

No fee is due in connection with this Reply Brief. The Director is authorized to charge any fees that may be required, or to credit any overpayment to Deposit Account No. 02-1818. If such a withdrawal is made, please indicate the Attorney Docket No. 3712036-01326 on the account statement.

Respectfully submitted,

K&L GATES LLP

BY _____

Robert M. Barrett
Reg. No. 30,142
Customer No. 29157
Phone No. 312-807-4204

Dated: August 23, 2011